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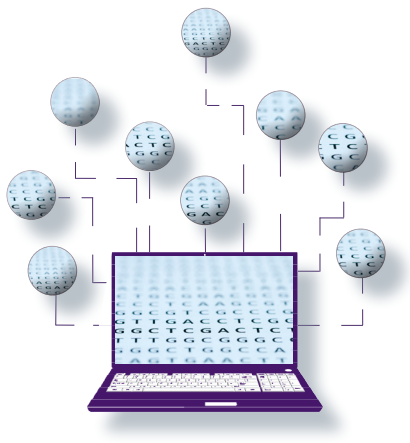
Sharing clinical genomic data for better diagnostics

Accurate determination of the genetic cause of a rare disease depends on the availability of knowledge about which mutations in a patient's genome could underlie their condition. As genomic research and analysis expands, this knowledge base is increasing rapidly but access to it, even within the National Health Service, is often severely restricted by inability or unwillingness to share this data across and even within institutions. This situation is incompatible with the delivery of high-quality, efficient, and reliable, genomic medicine in the NHS. The barriers to sharing genomic and clinical data must therefore be recognised and addressed as a matter of urgency.



Well executed whole genome analysis offers an unprecedented opportunity to determine the genetic basis of thousands of undiagnosed rare diseases, but a key bottleneck in delivery is the ongoing struggle to analyse and interpret complex and voluminous genome sequence data. This necessitates the comparison of a patient genome with current genomic, genetic and clinical data on the wider population and other patients with the same or similar illnesses. It is therefore essential for clinicians and scientists to have routine access to all existing information on the genetic variants and associated clinical characteristics relevant to their patient's disorder, in order to make the most informed interpretation and diagnosis.

This briefing explores the need for sharing genomic data within the NHS for delivering clinical genetic diagnoses, and sets out recommendations for addressing current barriers. Not covered here are the wider socio-political, ethical and regulatory concerns surrounding genomic and clinical data sharing within and beyond the NHS, which must also be addressed in order to balance safeguarding patient interests with advancing genomic medicine.

Current guidance on genomic data sharing:

Best practice guidelines followed by clinically accredited laboratories in the UK performing genetics tests recommend the submission of clinically relevant variants found by the lab to appropriate databases.[1-2]

The guidelines also note that *'complete upload of all variants and associated phenotype information from every patient is the ultimate goal'*, ideally via automated export functions.[2]

What are the barriers to sharing data within the NHS?

Despite recommendations within best practice guidelines [left] and efforts by a number of international initiatives advocating and encouraging sharing,[3-7] knowledge of genomic variants tends to be isolated in silos and data exchange between laboratories and deposition to existing public databases (*e.g.* DECIPHER, ClinVar, LoVD) is ineffective. The reasons for this situation include:

- **No prior urgency to share until now**
  Traditionally individual genetics laboratories have acquired specialist knowledge in distinct and non-overlapping disease domains and have not needed to share their findings more widely, since they are largely the sole consumers of that information in the UK.

- **Disincentives**
  Currently genetic testing services in the UK are in competition with each other to attract NHS referrals for testing and income. Knowledge generated by a given laboratory, might then be viewed as their intellectual property, which if distributed more widely would devalue the exclusivity of their service.

- **Overheads and absence of a sustainable solution**
  The logistical barriers to sharing data (time, resource overheads, and insufficient infrastructure) can, for many laboratories, outweigh the benefits reaped, particularly in the absence of a sustainable strategy for aggregating data from all diagnostic molecular genetics laboratories.

- **Social, regulatory and privacy concerns.**
  There are multiple and widespread social, legal and ethical concerns around the sharing of patients' personal genomic and clinical information.

Sharing genomic data – why is action needed now?

The promise of genomic medicine can only be realised by aggregating genomic data and knowledge. By enabling better data sharing now, the NHS can accomplish efficiency gains, patient benefits, and meet the target of becoming world leaders in genomic medicine.

The benefits to the NHS and patients of sharing genomic data:

- **More, faster, and more accurate diagnoses**
  Data sharing will increase the number of identified disease causing variants and knowledge of disease associated genes.

- **Improved equality of access**
  Better data sharing will improve the quality and efficiency of diagnosis across all NHS genetic testing facilities.

- **Benefits and savings across multiple NHS specialities**
  Patients with genetic disorders are also assessed in other clinical departments (*e.g.* cardiology, paediatrics, ophthalmology).

- **Better and more personalised treatment**
  More genomic data will better serve an ethnically diverse UK population, by improving knowledge on genetic diversity across different ethnic groups.
- **New medical and public health interventions**
  Underpinned by greater understanding of the relationship between genes and health.

The risks of not acting now:

- **'Diagnostic lottery'**
  Patients fail to receive diagnoses when their sample is referred to a laboratory that does not have access to information that could lead to their diagnosis.
- **Misdiagnosis**
  Leading to inappropriate treatment and care, because the clinician was unaware of critical information.
- **Missed resolution of cases**
  Where variants of unknown significance are not reclassified due to lack of information consolidation – prolonging a patient's wait for a diagnosis.
- **Inefficient use of resources**
  Resulting from multiple testing centres trying to reproduce knowledge that already exists within the NHS.
- **Opportunity cost**
  Failure to act now may have long-reaching effects.

What data needs to be shared?

All types of variants

Aggregating information on patient variants and clinical data is vital to discover significant links between specific variants and disease.

Sequence data

Essential to determine what 'normal' variation is within populations, and use this information to exclude the vast number of variants unlikely to be responsible for disease and improve the chances of finding 'true' variants in a patient's genome.

Phenotype and clinical information

Understanding the clinical context of a previously identified mutation and accessing detailed information on patients' disease characteristics and symptoms (phenotype) can help determine whether it is applicable to another case.

"Health and social care professionals should have the confidence to share information in the best interests of their patients...They should be supported by the policies of their employers, regulators and professional bodies"

Information governance review (2013)[8]

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Better data sharing for improved diagnosis: what next?

- The existing incentive structure undermines the objective of open data for wider public benefit. To gain buy-in and cooperation from all stakeholders, a system is needed where **all** NHS-funded genetic testing facilities are mandated to share their data with other (approved) laboratories.
- A NHS data resource for curating and sharing genomic data is an essential step towards ensuring long term sustainability and safeguarding patients' interests and trust.
- A data resource must serve the needs of clinicians to deliver better diagnosis, whilst being simple to use and to contribute to. Stakeholders must therefore work together to establish an effective solution.
- An NHS genomics repository should have the capacity to interact with the infrastructure created by the 100,000 Genomes Project. Consideration should be given to whether consent for this data sharing might be sought upfront, to ensure timely access to data; transparency with patients about the use of their genomic data is imperative.
- In order to affect change and attain widespread acceptability of the collection of patients clinical and genomic information, data privacy, confidentiality and ownership concerns must be managed appropriately.
- Leadership and strategic oversight are required for the successful, coordinated delivery of a data resource and compliance with data sharing, and these must therefore be established.
- Delivery of an improved sharing infrastructure will require investment, yet will generate cost savings and substantial benefit to patients and the NHS in the long run. NHS providers and commissioners must cooperate to devise a feasible, fair and sustainable funding mechanism.

Summary

Widespread sharing of genetic and clinical data within the NHS is necessary to fully realise the benefits of genomic medicine.

Failure to take action now will have undesirable consequences for patients and the NHS. Conversely, a timely solution will have far-reaching benefits, and help position the UK at the forefront of genomic medicine.

References

[1] Wallis Y *et al.*, ACGS (2013); [2] Ellard S *et al.*, ACGS (2014); [3] Clinvitae database: http://clinvitae.invitae.com/ ; [4] The Global Alliance for Genomics and Health http://genomicsandhealth.org/ ; [5] Human Variome Project: www.humanvariomeproject.org/ ; [6] International Collaboration for Clinical Genomics www.iccg.org/about-the-iccg/clingen/ ; [7] Free the data www.free-the-data.org; [8] The information governance review (2013).

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